

Criteria for requesting upper digestive Endoscopy in the diagnosis of dyspeptic Syndrome: A literature review

Edimundo Da Silva Quadros Júnior*¹, Ruana Farias Novaes¹, Ísis Nascimento Brandão¹, Gustavo Silveira Costa², Milton Costa Santana Filho², Bernardo Rodrigues Costa Coelho Sales³, Giovana Menezes de Resende Vieira³, Caique Caires Lima⁴, Saiane Menezes Moreira⁴, Lisandra Maria Costa Lago⁴, Lucas Davi Silva Veloso⁵, Maria Isabella Silva Abreu⁵, Maria Luiza de Azevedo Feitosa Fonseca⁶, Anselmo Messias Ribeiro da Silva Júnior¹

¹Medical Course, Santo Agostinho School of Health, Vitória da Conquista, Brazil.

²Medical Course, University Center Faculty of Technology and Sciences, Salvador, Brazil.

³ Medical Course, Imepac University Center, Araguari, Brazil.

⁴ Medical Course, Salvador University, Salvador, Brazil.

⁵ Medical Course, University Center FipMoc, Montes Claros, Brazil.

⁶ Medical Course, FIPGuanambi, Guanambi, Brazil.

edimundoquadros@hotmail.com

*Corresponding author.

Received: 21 Jan 2021;

Received in revised form:

06 Mar 2021;

Accepted: 03 Apr 2021;

Available online: 28 Apr 2021

©2021 The Author(s). Published by AI Publication. This is an open access article under the CC BY license

(<https://creativecommons.org/licenses/by/4.0/>).

Keywords— *Diagnostic investigation. Endoscopy. Alarm signs.*

Abstract— *Dyspepsia is defined by any disorder of digestion in the gastrointestinal tract or gastric sensitivity, and is divided into two groups: secondary dyspepsia, which are specific lesions such as peptic ulcer, esophagitis, gastric cancer, and cholelithiasis that result from different diseases, and functional dyspepsia. For the diagnosis of functional dyspepsia, the Rome IV criteria should be adopted. For the diagnosis of functional dyspepsia, the patient must have one or more of the following symptoms: a nagging sensation of postprandial fullness, early satiety, epigastric burning, and no evidence of structural disease that would explain the symptoms. There are signs and symptoms that the physician must be alert to in order to investigate more serious diseases that require earlier therapeutic measures, such as neoplasms. These signs are characterized as "alarm signals" and among them are, for example: unintentional weight loss, dysphagia, odynophagia, persistent vomiting, hematemesis, family history of cancer of the gastrointestinal tract. The use of upper endoscopy is one of the most common methods for investigating dyspepsia, but it should not be requested for all patients indiscriminately. Given this, the objective of this research was to identify the alarm signs and analyze the main criteria used for the request of upper gastrointestinal endoscopy in dyspeptic patients in order to reduce the impacts before the investigation and clinical management performed. For this, a systematic review of the literature was performed from a search in the Scielo database, using the descriptors "upper digestive endoscopy" and "dyspepsia", finding a total of 15 studies published in the period 2010 to 2020 and after reading the title and abstract, 14 articles were selected for presenting greater relevance and affinity with the subject under study. The inclusion criteria used were productions in the public domain that dealt with the proposed theme, works written in several languages and productions available in full, thus excluding the*

documents that did not meet the above criteria. The literature analysis allowed us to identify the main alarm signs and to identify the criteria used to request upper digestive endoscopy.

I. INTRODUCTION

Dyspepsia is any disorder of secretion, gastrointestinal motility, or gastric sensitivity that interrupts digestion and designates any changes related to the digestive system (MARÍA ET AL., 2018). It is generally benign and curable. The origin is not known, but it may be linked to emotional factor or disorder; and, in some cases, it may be due to a tumor process. According to Luporini et al., (2020), the ROMA IV consensus criteria classify dyspepsia as having an organic cause and a specific cause.

According to Leite et al. (2020), dyspeptic symptoms affect about one-third of the world's population and about 25% of dyspeptic patients have an associated organic cause. In contrast, most of these individuals have functional dyspepsia (FD), with symptoms arising from the gastroduodenal region in the absence of any explanatory organic disease.

Dyspepsia can still be characterized by pain or discomfort in the abdomen, affecting at least 20% of the world population and has multiple causes that can be benign or malignant pathologies. It is worth pointing out that when this discomfort/pain has not yet been studied, it is called uninvestigated dyspepsia (ZULETA et al., 2019).

The investigation of dyspepsia in primary care is one of the key points for reducing the consequences caused by its signs and symptoms. In addition, the need to investigate properly, requesting the necessary tests to qualified personnel, is of utmost importance for the conclusion of the diagnosis and treatment. (STANGHELLINI et al., 2016).

There are studies showing that the prevalence of uninvestigated dyspepsia can range from 7% to 45% worldwide. In addition, about 20-40% of the world's population has some dyspeptic complaint, such as epigastric pain, postprandial discomfort, and heartburn. (HYUK et al, 2014). The approach to adult patients can be of several forms, among which is the upper digestive endoscopy.

Upper digestive endoscopy is one of the most used exams for the investigation of dyspeptic patients; however, the choice of the procedure must take into consideration, for example, factors such as age and alarm signs, since these factors are important for the realization of differential diagnoses, such as neoplasms (MCNICHOL ET AL, 2012). Besides this, when selecting the patient, the risks must also be evaluated, even if minimal, because there are

diseases and morbid conditions that can be contraindications and that can even make the exam difficult (BAJAJ ET AL, 2020).

In this context, the objective of this study is to identify the alarm signs and analyze the main criteria used to request upper gastrointestinal endoscopy in dyspeptic patients in order to reduce the impacts on the investigation and clinical management performed.

II. MATERIAL AND METHODS

This work is a systematic review of literature of a descriptive nature, with a qualitative approach, which focuses on the knowledge produced and published in books, journals and articles about the criteria used to request upper digestive endoscopy in dyspeptic patients' records. It is worth pointing out that bibliographical research is a fundamental step in all scientific work that will influence all the stages of research, aiming to compare studies that can reach a conclusion or provide new lines of thought within the theme addressed.

Thus, a bibliographical survey was carried out in Scielo databases, using the following descriptors in English: upper digestive endoscopy AND dyspepsia.

In the search, 15 studies were found, published in the period from 2010 to 2020, and after reading the title and abstract, 14 articles were selected for presenting greater relevance and affinity with the theme under study. The inclusion criteria used were productions in the public domain that dealt with the proposed theme, works written in several languages and productions available in full, thus excluding the documents that did not meet the above criteria.

III. RESULTS AND DISCUSSION

Dyspepsia is according to María (2018), any functional alteration of the digestive system that is generally benign and curable. It is further defined as any disturbance of digestion either by disturbance of secretion, gastrointestinal motility or gastric sensitivity. Dyspepsia is divided into two groups: a secondary one that is defined by specific lesions, such as peptic ulcer, esophagitis, gastric cancer, and cholelithiasis that result from distinct diseases, and functional dyspepsia (RAMIREZ-VASQUEZ, 2018). According to Leite (2020), these symptoms affect about one third of the world's population.

According to Mikito (2010), dyspepsia is defined as digestion disorders in the upper gastrointestinal tract and has symptoms such as pain, burning in the abdominal region, postprandial stuffiness, nausea, vomiting and abdominal distension, which may or may not be related to food or stress. However, when in the diagnosis, it is not possible to identify the cause by the symptoms, there is the functional dyspepsia, which is characterized by periods of slowdowns and exacerbations. Some of the symptoms that may have associations with functional

dyspepsia are: chronic or recurrent pain, burning or discomfort, nausea, vomiting, and abdominal distension.

Thus, it is important to identify the alarm signs and analyze the main criteria used to request upper gastrointestinal endoscopy in dyspeptic patients. Therefore, table 1 shows a summary of the articles selected with the respective authors, journal published, and year of publication (Table 1).

*According to its source language

Table 1 – Studies addressing alarm signs and criteria for requesting upper endoscopy.

Title	Authors	*Journal/Year		
Endoscopic and Histopathological Patterns in Modcoicar et al. Dyspeptic Patients at the Maputo Central Hospital, Mozambique		Jornal	Português	de
		Gastreterologia/2011		
Comparison of sequential therapy with standard Zuleta et al. triple therapy in the eradication of Helicobacter pylori		Jornal	Português	de
		Gastreterologia/2011		
Sensitivity of gastric biopsy in detecting Azaña et al. Helicobacter pylori in patients treated with proton pump inhibitors		Revista Médica Herediana/2012.		
Relatives of gastric cancer patients have a high Zuleta et al. frequency of hypochlorhydria and premalignant gastric lesions		Revista	Colombiana	de
		Gastroenterología/2014.		
Double-pylorus in the era of proton pump inhibitors	Mansur et al.	Revista de Gastroenterología	del	
		Perú/2014.		
A day of upper digestive endoscopy in a Areia et al. southern European country		Jornal	Português	de
		Gastreterologia/2014.		
Approach to the patient with dyspepsia and Otero et al. functional dyspepsia: update		Revista	Colombiana	de
		Gastroenterología/2014.		
Early vs. gastric cancer advanced: are there any differences?	Gomez et al.	Revista de la Universidad Industrial de Santander. Salud		
		/2015.		
Gastric xanthomas are associated with malignant and Alonso et al. premalignant injuries		Revista	Colombiana	de
		Gastroenterología/2015.		
Validation of the rapid urease test for the Idelfonso et al. detection of Helicobacter pylori at the Hospital Nacional Cayetano Heredia, Lima, Peru.		Revista de Gastroenterología del Perú/2017.		
Morphological changes of the upper Amorim et al. gastrointestinal tract in patients with new onset dermatomyositis: correlation with		Medical Express/2017.		

demographic, clinical and laboratory characteristics	
Endoscopic dissection of the submucosa in the Ughelli et al. treatment of initial esophageal cancer	Revista de Gastroenterología del Perú/2017.
Association of duodenal eosinophilic infiltrate Leite et al. with <i>Helicobacter pylori</i> infection, but not with functional dyspepsia	Arquivos de Gastroenterologia/2020.
Malignant peritoneal mesothelioma as a rare Sousa et al. cause of dyspeptic complaints and ascites: a diagnostic challenge	GE – Jornal Português de Gastreenterologia/2020.

Dyspepsia symptoms have a high prevalence in the population and represent a large number of important causes of Primary Health Care consultations, which bring high costs of a socioeconomic nature and a major health care problem (MODCOICAR ET AL., 2011).

According to the aforementioned authors, there is a direct relationship between patients with dyspeptic complaints and *Helicobacter pylori* infection. This infection is more common in developing countries, with poverty being one of the most important factors for its spread. The routes of transmission can be oro-oral, gastrooral, or feco-oral. It can be acquired during childhood associated with facilitated transmission conditions, in addition to gastric diseases such as chronic gastritis, peptic ulcer disease, lymphomas, and gastric cancer.

H. pylori is an agent involved in a large number of gastrointestinal pathologies. According to Zuleta et al (2011), it affects more than 50% of the world's population and its prevalence is higher in developing countries.

In the above work, patients with functional dyspepsia who had not received previous *H. pylori* eradication treatment, aged between 19 and 70 years were referred for upper digestive endoscopy, and soon after the confirmation of the etiologic agent, the patients were randomized through a list to receive two treatments which were: A1- Omeprazole 40 mg/day + clarithromycin 1 g/day + amoxicillin 1 g/day. And A2- Omeprazole 40 mg/10 days + amoxicillin 2g/5 days. In the last five days, amoxicillin was replaced by tinidazole 1g/day + clarithromycin 1 g/day.

Nevertheless, in both treatments, low success was found, according to the author, it may have been because of the use of generic drugs, indicating the need for conducting similar studies with reference drugs, in addition to antimicrobial resistance in the studied population. Despite this, Chaves et al. (2017) showed no

differences in the efficacy of reference and generic drugs when comparing the activity of azithromycin.

According to Azaña et al. (2012), one of the most frequent reasons for visits to the health service is chronic pain or discomfort defined as dyspepsia, recurrent in the upper abdomen. There are some strategies proposed for the treatment of dyspepsia such as the use of empirical therapy like H₂ receptor antagonists and proton inhibitors, the use of non-invasive tests or referral for endoscopy. According to the author, there is a worldwide prevalence of 65% of *Helicobacter pylori* infection.

According to Zuleta et al. (2014), there are several alarm symptoms that may suggest presences of a tumor or complicated organic disease, some of the symptoms are: upper abdominal pain relieved by defecation associated with change in stool (either in color or shape), upper pain that bothers/worsens with eating, weight loss, anemia/digestive bleeding, and dysphagia. According to the author, the main approaches followed in patients with PD are: immediate endoscopy when there are alarm signs/symptoms, empirical treatment with antisecretory drugs, and investigation and treatment for *Helicobacter pylori* when positive.

According to Mansur et al. (2014), gastrointestinal abnormalities can be found during upper digestive endoscopy, with double pyloric disease being a rare, relatively benign abnormality with a prevalence between 0.06% and 0.4% and often associated with peptic ulcer of the stomach or duodenum, diseases of the respiratory system, chronic renal disease, or diabetes mellitus. Moreover, according to the author, *H. pylori* eradication is recommended because it prevents the formation of new ulcers and improves fistula healing.

According to Areia et al. (2014), upper digestive endoscopy is poorly described and the data found are poorly reflected in clinical decisions, besides being a relevant option for surveillance of asymptomatic high-

risk patients. In addition, the most frequent indications for this type of examination were presence or suspicion of bleeding (20%), abdominal pain or dyspepsia (18%) or reflux (12%). In a study conducted where a high prevalence of gastric lesions and *H. pylori* was expected, positivity for *H. pylori* was found to be present in 38% (95% CI: 25-51%) meaning that two-fifths of the population are positive for *H. pylori*. According to Areia, decision analysis studies are needed to evaluate upper endoscopy as a surveillance option for these asymptomatic patients at risk.

According to Zuleta et al., (2014), gastric cancer (GC) is a pathology that has a major impact on global morbidity, its prognosis is poor, as it has a survival rate of less than 10% in most patients. Intestinal gastric cancer is the most common, and has more risk factors identified, such as infection by *H. pylori* that is the etiologic agent in at least 90% of cases, so early detection through upper digestive endoscopy is extremely important.

The eradication of infection should be verified by non-invasive methods, such as respiratory test for urea or fecal antigens, four weeks after the end of the antibiotic, the author also mentions that some drugs are effective and recommended for the treatment of DF, but the studies are still few (ZULETA ET AL., 2014).

According to Gomez et al., (2015), gastric cancer has a high prevalence and mortality in Colombia, it is the fourth most present cancer worldwide, and when detected early, once the survival is 5 years in the neoplasm group is almost 100%, whereas advanced gastric has a survival of almost 10% and the diagnostic method for detection is high digestive endoscopy, but unfortunately in several countries less than 5% of patients are detected at an early stage. Furthermore, the study showed that in patients with uninvestigated dyspepsia, gastric cancer was found in 9% of patients, according to the author, in patients with dyspepsia, the detection rate of lesions by upper digestive endoscopy confers a better prognosis.

Gomez et al (2015), in another paper, cites another comorbidity, gastric xanthomas, which are gastrointestinal lesions, incidentally found in upper digestive endoscopy in the mucosa of any part of the gastrointestinal tract, but are more frequent in the stomach, is associated with increasing age of the patient, and in some cases, the origin of xanthomas although uncertain, may be linked to chronic gastritis, *H. pylori* infection and diabetes mellitus, do not produce definite symptoms. Previously, it was very rare, but with the massification of upper digestive endoscopy, there are more and more reports. In the study by Alvaro et al, *H. pylori* infection was found in 42.3% of the patients, in the

work of Hori et al, they observed almost this same rate of infected, in which infection was observed in 48% of a total of 145 patients (GOMEZ ET AL, 2015).

For patients with dyspeptic symptoms, the diagnosis of *H. pylori* infection, which initially is a superficial process, and may worsen to what is called chronic active gastritis, can be made by various methods requiring endoscopy, which are grouped into 2 types: the invasive ones, such as histopathological studies, the high urease test (HUR), culture and polymerase chain reaction; and the non-invasive ones, the breathalyzer test, serology and stool antigens (IDELFONSO ET AL., 2017).

Dermatomyositis (DM), is a rare systemic autoimmune disease, which is characterized by systemic proximal, symmetrical, progressive limb weakness and the presence of typical skin lesions. Presenting symptoms are constitutional, joint, cardiac, pulmonary, and gastrointestinal tract involvement. When the upper gastrointestinal tract is affected in patients with DM, they may be asymptomatic or have symptoms such as dysphagia, heartburn, nausea, vomiting, abdominal distension, and upper abdominal pain (AMORIM ET AL., 2017). Moreover, according to Amorim et al. (2017), the management and guidance of these gastrointestinal disorders in the sample performed of patients with DM relate to upper digestive endoscopy, focused on the need for prevention of esophageal and gastroduodenal lesions in these patients besides being relevant to guide potential digestive changes.

In a study of an 80-year-old patient with a oneyear history of dyspepsia who had esophageal lesions that were identified by endoscopy, and the use of chromoendoscopy, the author mentions that upper digestive endoscopy can be used as control and follow-up so that the lesions are treated at an early stage (UGHELLI, 2017). Moreover, according to Ughelli et al., (2017), by means of upper digestive endoscopy, one can diagnose patients with neoplastic lesions achieving definitive, safe and effective treatment, although it is not free of complications such as risk of perforation, hemorrhage and emphysema.

Functional dyspepsia is a multifactorial disease, in which about one third of the world population has dyspeptic symptoms (LEITE ET AL, 2020). *H. pylori* infection is very common in southern Brazil, and it may be directly associated with functional dyspeptic patients. The hypothesis of DF etiology may include gastroduodenal motility disorders, gastric hypersensitivity, *H. pylori* infection (leading to pain, muscle spasms), and psychosocial distress, but must be

adapted from person to person. *H. pylori* infection, affects more than two thirds of functional dyspeptic patients. According to the author, different populations are influenced by local genetics and microbiota, and these factors directly influence.

According to Sousa et al., (2020), malignant peritoneal mesothelioma is a rare disease of the cells of the peritoneum, and pleural mesotheliomas are the most frequent. In the early stages of the disease, clinical manifestations are nonspecific, approximately 8% of patients are diagnosed accidentally. The patient evaluated in this case, was a 53-year-old male, a former smoker, with a previous 5-year exposure to asbestos and who had a family medical history of mesothelioma. The patient who was initially evaluated, reported 3 months of dyspeptic complaints (abdominal pain, early satiety, nausea and vomiting). Upper digestive endoscopy revealed *H. pylori* microorganisms.

ACKNOWLEDGMENT

This research was supported by Faculdade de Saúde Santo Agostinho.

REFERENCES

- [1] A.A. María, M. Virgen et al. Eficacia del masaje tuina en pacientes con dispepsia funcional. *Consultorio 24*. Enero 2018 - Febrero 2019. *Multimed*, v. 24, n. 1, p. 50–69, 2018.
- [2] A.M. Gómez, J. Humberto et al. Cáncer gástrico temprano vs. avanzado: ¿existen diferencias? *Revista de la Universidad Industrial de Santander. Salud*, v. 47, n. 1, p. 7–13, 2015.
- [3] A. María, A. Oliva et al. Eficacia del masaje tuina en pacientes con dispepsia funcional. *Consultorio 24*. Enero 2018 - Febrero 2019. *Multimed*, v. 24, n. 1, p. 50–69, 2018.
- [4] C. Leite, E.L. Mazzonoleni et al. Association of duodenal eosinophilic infiltrate with helicobacter pylori infection, but not with functional dyspepsia. *Arquivos de Gastroenterologia*, v. 57, n. 1, p. 74–78, 2020.
- [5] D. Azaña, M. Egoavil, et al. Sensibilidad de la biopsia gástrica en la detección de *Helicobacter pylori* en pacientes en tratamiento con inhibidores de la bomba de protones. *Revista Medica Herediana*, v. 23, n. 1, p. 11–15, 2012.
- [6] L. Ughelli, C. Miranda et al. Disección endoscópica submucosa en el tratamiento del cáncer precoz de esófago. *Revista de Gastroenterología del Perú*, v. 37, n. 4, p. 365–369, 2017.
- [7] M. Areia. One day of upper gastrointestinal endoscopy in a southern European country. *GE Jornal Português de Gastreenterologia*, v. 21, n. 3, p. 97–101, 2014.
- [8] N. Matsuda, MAIA, C. C. et al. Dispepsia funcional: revisão de diagnóstico e fisiopatologia. *Diagn. tratamento*, v. 5, n. 1, p. 35–39, 2010.
- [9] N.Mitikito, C. Matsuda et al. Interesse geral Dispepsia funcional: revisão de diagnóstico e fisiopatologia Interesse geral. v. 15, n. 3, p. 114–120, 2010.
- [10] P. Modcoicar, J. Arteaga et al. Padrão Endoscópico e Histo-Patológico em Doentes Dispépticos no Hospital Central de Maputo-Moçambique. *Jornal Português de Gastreenterologia*, v. 18, n. 5, p. 226–229, 2011.
- [11] R. Otero, W.G. Zuleta et al. Enfoque del paciente con dispepsia y dispepsia funcional: actualización. *Revista Colombiana de Gastroenterologia*, v. 29, n. 2, p. 132–138, 2014.
- [12] R.A. Silva, T.R. Pinheiro et al. Dispepsia [23] J.S. Bajaj, et al. "Major Trends in funcional e depressão como fator Gastroenterology and Hepatology Between 2010 associado. *Arquivos de Gastroenterologia*, v. 43, and 2019: An Overview of Advances From the n. 4, p. 293–298, 2006. Past Decade Selected by the Editorial Board of: The American Journal.
- [13] R. Mansur, S.F. Souza et al. Doble píloro en la Gastroenterology." *American Journal of era de los inhibidores de la bomba de Gastroenterology 115.7* (2020): 1007-1018. protones. *Revista de Gastroenterología del Perú*, v. 34, n. 2, p. 139–140, 2014.
- [14] R. O. Gomez, W.M Buttrago. Los xantomos gástricos están asociados con lesiones malignas y premalignas. *Revista Colombiana de Gastroenterologia*, v. 30, n. 2, p. 151–156, 2015.
- [15] T.M. Amorim, C.K.F. Junior, et al. Morphological alterations of upper gastrointestinal tract in patients with new onset dermatomyositis: correlation with demographic, clinical and laboratory features. *Medical Express*, v. 4, n. 2, 2017.
- [16] Z.M. Gómez, D.N. Garzón, et al. Familiares de pacientes con cáncer gástrico tienen alta frecuencia de hipoclorhidria y de lesiones premalignas gástricas. *Revista Colombiana de Gastroenterologia*, v. 29, n. 1, p. 3–10, 2014.
- [17] Z.M. Gómez, C.B. Melgar et al. Comparación de la terapia secuencial con la triple terapia estándar en la erradicación de *Helicobacter pylori*. *Revista Colombiana de Gastroenterologia*, v. 26, n. 3, p. 171–177, 2011.
- [18] A.C.T.A. Chaves et al. Estudo comparativo da atividade antibacteriana de azitromicina em medicamentos de referência, genérico e similar. *REVISTA SAÚDE.COM*, v. 13, p. 2017, 2017.
- [19] R.L. Loporini, A.L. Lanza et al. Diagnosis and treatment of constipation: A clinical update based on the Rome IV criteria. *Journal of Coloproctology*, v. 40, n. 04, p. 425–426, 2020.
- [20] V. Stanghellini, F.K.L, Chan et al. Gastroduodenal Disorders. *Gastroenterology*, v. 150, n. 6, p. 1380–1392, 2016.
- [21] L. Hyuk, J. HYE-KYUNG, et al. Current status of functional dyspepsia in Korea; *Korean J Intern Med*. v. 29, n. 2, p. 156-165, mar. 2014

- [22] A.G. McNicholl, et al, Meta-analysis: esomeprazole or rabeprazole vs. first-generation pump inhibitors in the treatment of *Helicobacter pylori* infection, *Alimentary Pharmacology & Therapeutics*, v. 36, n. 5, p. 414–425, 2012.